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| 10/578,809 | 03/12/2007 | Jerome B. Zeldis | 9516-186-999 | 6157 |

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| EXAMINER |
|---|
| HUANG, GIGI GEORGIANA |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1612 | |

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|---|---|
| 07/21/2010 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/578,809 | ZELDIS, JEROME B. | |
| | Examiner | Art Unit | |
| | GIGI HUANG | 1612 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single compound as addressed below, to which the claims must be restricted.

The claims are directed to the use of a JNK inhibitor for treating, preventing and/or managing an asbestos-related disease or disorder in a patient. The claims do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking claims 1-29 is the use of a JNK inhibitor for treating, preventing and/or managing an asbestos-related disease or disorder in a patient.

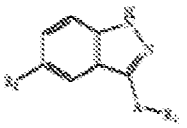
Buschmann et al. (WO 99/17798) teaches a method of treating tumor such as mesothelioma with an agent that inhibits the JNK signal (JNK inhibitor, Claims 12, 14, 20-22)

Therefore, the technical feature linking the claims lacks novelty and does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

Accordingly, the claims are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

2. This application also contains claims directed to more than one type of JNK formula of the generic invention. These different JNK formula genera are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1 as they have distinct formulas that do not share a common core.

The species are as follows:

a) 

or a pharmaceutically acceptable salt thereof,

wherein:

A is a direct bond, —$(CH_2)_a$—, —$(CH_2)_aCH$=$CH(CH_2)_b$—, or —$(CH_2)_aC$≡$C(CH_2)_b$—;

$R_1$ is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted with one to four substituents independently selected from $R_4$;

$R_2$ is —$R_5$, —$R_6$, —$(CH_2)_aC$(=O)$R_6$, —$(CH_2)_aC$(=O)$OR_6$, —$(CH_2)_aC$(=O)$NR_6R_7$, —$(CH_2)_aC$(=O)$NR_7(CH_2)_aC$(=O)$R_6$, —$(CH_2)_aNR_7C$(=O)$R_6$, —$(CH_2)_aNR_7C$(=O)$NR_6R_7$, —$(CH_2)_aNR_6R_7$, —$(CH_2)_aOR_6$, —$(CH_2)_aSO_2R_6$, or —$(CH_2)_aSO_2NR_6R_7$;

a is 1, 2, 3, 4, 5 or 6;

b and c are the same or different at each occurrence independently selected from 0, 1, 2, 3 or 4;

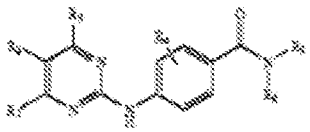
d is at each occurrence 0, 1 or 2;

$R_3$ is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, heterocycle, heterocycloalkyl, —C(=O)$OR_8$, —OC(=O)$R_8$, —C(=O)$NR_8R_9$, —C(=O)$NR_8OR_9$, —$SO_2NR_8R_9$, —$NR_8SO_2R_9$, —CN, —$NO_2$, —$NR_8R_9$, —$OR_8$, —$OC$(=O)$R_8$, —$NR_8C$(=O)$OR_9$, —$NR_8C$(=O)$(CH_2)_dOR_9$, —$NR_8C$(=O)$(CH_2)_dR_9$, —$OC(CH_2)_dNR_8R_9$, or heterocycle fused to phenyl;

$R_4$ is alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, each being optionally substituted with one to four substituents independently selected from $R_3$, or $R_4$ is halogen or hydroxy;

$R_5$, $R_6$ and $R_7$ are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl, wherein each of $R_5$, $R_6$ and $R_7$ are optionally substituted with one to four substituents independently selected from $R_3$; and $R_8$ and $R_9$ are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocycloalkyl, or $R_8$ and $R_9$ taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of $R_8$, $R_9$ and $R_8$ and $R_9$ taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from $R_4$,

,

b) 

or a pharmaceutically acceptable salt thereof,

wherein:

$R_1$ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from $R_{10}$;

$R_2$ is hydrogen;

$R_3$ is hydrogen or lower alkyl;

$R_4$ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl and lower alkoxy;

$R_5$ and $R_6$ are the same or different and independently $-R_{11}$, $-(CH_2)_nC(=O)R_{11}$, $-(CH_2)_nC(=O)OR_{11}$, $-(CH_2)_nC(=O)NR_{12}R_{13}$, $-(CH_2)_nC(=O)NR_{12}(CH_2)_nC(=O)R_{13}$, $-(CH_2)_nNR_{12}C(=O)R_{13}$, $(CH_2)_nNR_{12}C(=O)NR_{12}R_{13}$, $-(CH_2)_nNR_{12}R_{13}$, $-(CH_2)_nOR_{11}$, $-(CH_2)_nSO_2R_{11}$ or $-(CH_2)_nSO_2NR_{12}R_{13}$;

or $R_5$ and $R_6$ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

$R_7$ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, aryloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, arylalkyl, heterocycle, heterocycloalkyl, $-C(=O)OR_{11}$, $-OC(=O)R_{11}$, $-C(=O)NR_{12}R_{13}$, $-C(=O)NR_{12}OR_{11}$, $-SO_2R_{11}$, $-SO_2NR_{12}R_{13}$, $-NR_{12}SO_2R_{11}$, $-NR_{12}R_{13}$, $-NR_{12}C(=O)R_{11}$, $-NR_{12}C(=O)(CH_2)_nOR_{11}$, $-NR_{12}C(=O)(CH_2)_nR_{11}$, $-(CH_2)_nNR_{12}R_{13}$, or heterocycle fused to phenyl;

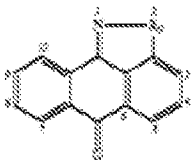
$R_{10}$, $R_{11}$, $R_{12}$ and $R_{13}$ are the same or different and at each occurrence independently hydrogen, alkyl, substituted alkyl, aryl, arylalkyl, heterocycle or heterocycloalkyl;

or $R_{12}$ and $R_{13}$ taken together with the atom or atoms to which they are attached to form a heterocycle;

n and k are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.

, and

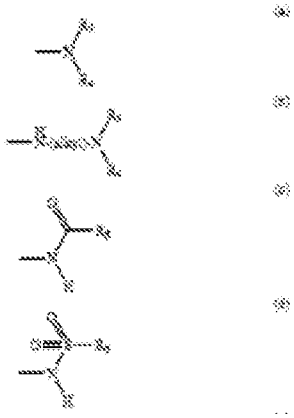


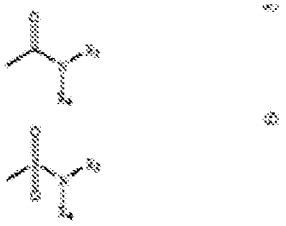
or a pharmaceutically acceptable salt thereof,

wherein $R_x$ is —O—, —S—, —S(O)—, —$S(O)_2$—, NH or —$CH_2$—;

the compound being (i) unsubstituted, (ii) monosubstituted and having a first substituent, or (iii) disubstituted and having a first substituent and a second substituent;

the first or second substituent, when present, is at the 3, 4, 5, 7, 8, 9, or 10 position, wherein the first and second substituent, when present, are independently alkyl, hydroxy, halogen, nitro, trifluoromethyl, sulfhenyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono-alkylaminoalkoxy, di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c), (d), (e), or (f):



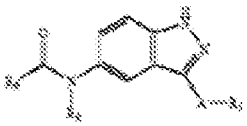


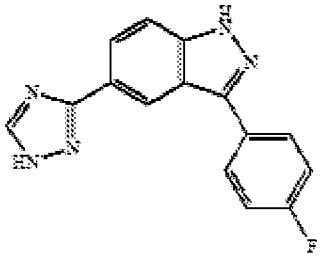
wherein $R_3$ and $R_4$ are taken together and represent alkylidene or a heteroatom-containing cyclic alkylidene or $R_3$ and $R_4$ are independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, arylcarbonylalkyl, alkoxyalkyl, aminoalkyl, mono-alkylaminoalkyl, or di-alkylaminoalkyl; and

$R_5$ is hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, alkoxyalkyl, alkoxycarbonylalkyl, amino, mono-alkylamino, di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, cycloalkylalkylamino, aminoalkyl, mono-alkylaminoalkyl, or di-alkylaminoalkyl.

c)

It is noted that the formulas also contain numerous subgenera that create different cores from each other and within them a multitude of compounds within the

subgenera. An example is formula b) where  is a different



subgenus structure than ,

another example is formula c) where $R_0$ can be –O-, -S-, -S(O)-, -$S(O)_2$-, -NH, or -$CH_2$-, wherein when $R_0$ is –S-, it represents a different core than when $R_0$ is -$CH_2$-, where they are two different cores and have no unity as a result.

Applicant is required, in reply to this action, to elect a single JNK formula genera to which the claims shall be restricted if no generic claim is finally held to be allowable, and Applicant is further required to elect a single specific compound from within the elected formula for examination. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise require all the limitations of an allowed generic claim. Currently, the following claim(s) are generic: claim 1 and 29.

## REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

## WHEN CLAIMS ARE DIRECTED TO MULTIPLE CATEGORIES OF INVENTIONS

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

3. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a JNK formula and an election of a single specific compound species of the JNK formula elected to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention or species.

Should applicant traverse on the ground that the inventions have unity of invention (37 CFR 1.475(a)), applicant must provide reasons in support thereof. Applicant may submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. Where such evidence or admission is provided by applicant, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GiGi Huang/
Examiner, Art Unit 1612
/Zohreh A Fay/
Primary Examiner, Art Unit 1612